

**Summary Minutes of the
Pulmonary-Allergy Drugs Advisory Committee (PADAC)
November 19, 2009
Hilton Washington, DC/Silver Spring
The Ballrooms, 8727 Colesville Road, Silver Spring, Maryland**

All external requests for the meeting transcript should be submitted to the CDER, Freedom of Information office.

**These summary minutes for the Pulmonary-Allergy Drugs Advisory Committee meeting of the Food and Drug Administration were approved on
_____1/7/10_____**

I certify that I attended the November 19, 2009 meeting of Pulmonary-Allergy Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

**_____/s/_____
Kristine Khuc, Pharm.D.
Designated Federal Official,
PADAC**

**_____/s/_____
Mark Brantly, M.D.
Acting Committee Chair,
PADAC**

FOOD AND DRUG ADMINISTRATION (FDA)
Pulmonary-Allergy Drugs Advisory Committee (PADAC)
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The following is an internal report which has not been reviewed. A verbatim transcript will be available in about 6 weeks, sent to the Division of Pulmonary-Allergy Products and posted on the FDA website at:

<http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Pulmonary-AllergyDrugsAdvisoryCommittee/ucm126203.htm>

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The Pulmonary-Allergy Drugs Advisory Committee (PADAC) met on November 19, 2009 at the Hilton Washington DC/Silver Spring, The Ballrooms, 8727 Colesville Road, Silver Spring, Maryland. Prior to the meeting, the members and the invited consultants had been provided the background material from the FDA. The meeting was called to order by Mark Brantly, M.D., (Acting Chair); the conflict of interest statement was read into the record by Kristine Khuc, Pharm.D. (Designated Federal Official). There were approximately 120 persons in attendance. There were no speakers for the Open Public Hearing session.

Attendance:

Pulmonary-Allergy Drugs Advisory Committee Members Present (Voting):

Leslie Hendeles, Pharm.D., Richard Honsinger, M.D., Daren Knoell, Pharm.D., Thomas Alexander Platts-Mills, Ph.D., Peter Terry, M.D.

Drug Safety and Risk Management Advisory Committee Member Present (Voting):

Sidney Wolfe, M.D. (Consumer Representative)

Special Government Employee Consultants Present (Temporary Voting Members):

Mark Brantly, M.D. (Acting Chair), Sean Hennessy, Pharm.D., Ph.D., Andrea Holka (Patient Representative), Timothy Lesar, Pharm.D., Lee Newman, M.D., David Schoenfeld, Ph.D.

FDA Participants Present (Non-Voting):

Curtis Rosebraugh, M.D., Badrul Chowdhury, M.D., Ph.D., Solomon Iyasu M.D., Theresa Michele, M.D.

Designated Federal Official:

Kristine Khuc, Pharm.D.

Issue:

To discuss efficacy supplement for new drug application (NDA) No. 21-395 for the approved product Spiriva HandiHaler (tiotropium inhalation powder), manufactured by Boehringer Ingelheim for the reduction in exacerbations (worsening of symptoms) in patients with chronic obstructive pulmonary disease (COPD)

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The Agenda was as follows:

Call to Order	Mark Brantly, M.D.
Introduction of Committee	Acting Chair, PADAC
Conflict of Interest Statement	Kristine Khuc, Pharm.D., Designated Federal Official, PADAC
Opening Remarks	Badrul Chowdhury, M.D., Ph.D. Director, Division of Pulmonary and Allergy Products, Center for Drug Evaluation and Research (CDER)

Sponsor Presentation

Introduction	Thor Voigt, M.D. Senior Vice-President, Medicine and Drug Regulatory Affairs Boehringer Ingelheim Pharmaceuticals, Inc.
COPD and the Importance of Exacerbations	Donald Tashkin, M.D. Professor of Medicine David Geffen School of Medicine at UCLA
Clinical Data	Steven Kesten, M.D. Vice President, Medicine Marketed Products Respiratory, Boehringer Ingelheim Pharmaceuticals, Inc.

Questions to Sponsor for Clarification

Break

FDA Presentation

Efficacy and Safety Considerations	Theresa M. Michele, M.D. Medical Officer, Division of Pulmonary and Allergy Products CDER, FDA
Statistical Perspective	Joan Buenconsejo, Ph.D. Mathematical Statistician, Division of Biometrics II CDER, FDA

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Epidemiology Data

Simone Pinheiro, Sc.D.
Epidemiologist, Division of Epidemiology
CDER, FDA

Questions to FDA for Clarification

Lunch

Open Public Hearing

Charge to Committee

Sally Seymour, M.D.
Deputy Director for Safety, Division of
Pulmonary and Allergy Products
CDER, FDA

Discussion of Questions/Vote

Adjourned at approximately 3:15 p.m.

Questions to Committee:

1. Please comment on the mortality data from Spiriva HandiHaler trial 205.235 (UPLIFT). (Discussion- *See below*)
2. Please comment on the mortality data from the Spiriva Respimat Phase 3 trials (205.254, 205.255, and 205.372). (Discussion- *See below*)

Discussions for Question 1 and Question 2 were combined together.

Committee members had the following comments:

- *UPLIFT trial data was adequate*
- *Trial design for UPLIFT showed improvement in mortality*
- *Data from UPLIFT is compelling and suggests that there is not an increase in mortality*
- *Concerns of dose response and cardiovascular effects seen in the Respimat trial*
- *Concern whether the population studied is truly representative of the real world population*
- *Still unclear as to what the shorter trial Respimat data is suggesting*
- *Further looking at studies to assess quality of life and not just survival*

(Please see transcript for detailed discussion)

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3. Do the data from trials 205.235 (UPLIFT) and 205.266 (VA study) provide substantial and convincing evidence to support the claim that Spiriva HandiHaler reduces COPD exacerbations? (Voting question)

YES= 11 NO= 1 ABSTAIN= 0

a.) If not, what additional data are needed?

Committee members stated the need to obtain:

- *Studies on inflammatory indices to see if there is a direct or indirect effect on exacerbations*
- *Exact mechanism of action of exacerbations*
- *Look at other modalities to include pulmonary rehabilitation*

(Please see transcript for detailed discussion)

4. Do the data from trial 205.235 (UPLIFT) adequately address the potential safety signal of stroke events? (Voting question)

YES= 11 NO= 1 ABSTAIN= 0

a.) If not, what additional data are needed?

Most committee members agreed that the UPLIFT trial data was adequate to address the safety signal of stroke events and no further studies are needed.

(Please see transcript for detailed discussion)

5. Do the data from trial 205.235 (UPLIFT) adequately address the potential safety signal of adverse cardiovascular outcomes? (Voting question)

YES= 11 NO= 0 ABSTAIN= 1

a.) If not, what additional data are needed?

The vast majority of the committee members felt that the data was convincing and strong enough to adequately address this safety signal.

(Please see transcript for detailed discussion)